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Depolarization Changes Early in the Course of Myocardial Infarction: Significance of Changes in the Terminal Portion of the QRS Complex

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Studies of patients during variant angina have revealed that there are specific changes in the terminal part of the QRS complex that provide information regarding the location of the ischemia. Extending these studies to acute myocardial infarction, the electrocardiogram (ECG) obtained from 32 patients within 5 h of the onset of chest pain was analyzed to determine if similar inferences could be made. A preinfarction ECG was available from each patient for comparison and 30 patients underwent coronary arteriography within 3 weeks of the infarction.

The 10 patients with anterior infarction had a decrease ($p < 0.05$) in the S wave in leads V_2 (0.80 ± 0.50 mV) and V_3 (0.65 ± 0.43 mV). In 23 patients with inferior infarction an increase ($p < 0.05$) in the R wave of lead III (0.47 ± 0.35 mV), S wave of lead aVL (0.31 ± 0.23 mV) and R wave of lead aVF (0.37 ± 0.30 mV) occurred. A strong positive correlation between the R wave changes in leads III and aVF and the S wave in lead aVL ($r = 0.94$ and 0.91, respectively) suggests that the R and S wave changes in these leads are expressions of the same phenomenon and indicates that the terminal QRS complex is chiefly affected.

Eight of 23 patients with inferior infarction and ST depression in the anterior precordial leads had a normal left anterior descending coronary artery. All had an increase in S wave amplitude in leads V_2 and V_3. Eight patients had inferior infarction, ST depression in anterior leads and severe lesions in the left anterior descending artery or anterior wall motion abnormalities. These patients had variable changes in the S wave amplitude in leads V_2 and V_3 (in four patients the S waves increased; in four the S waves decreased, a response usually seen in anterior infarction). Two of the four patients with decreased S wave in leads V_2 and V_3 died after a subsequent anterior infarction.

It is concluded that QRS changes early in the course of acute myocardial infarction are similar to those occurring during variant angina and are due to decreased intramyocardial conduction velocity in the ischemic region. Analysis of the terminal portion of the QRS complex early during infarction has value in determining the location of the ischemic zone.

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We have observed that myocardial ischemia alters the QRS complex in a predictable manner in patients with variant angina and similar changes have been noted during transient ischemia in dogs (1). The QRS changes consist of a modest prolongation of QRS duration and a change in the voltage of the terminal portion of the QRS complex that can be represented by a vector directed toward the ischemic zone. Conduction velocity measurements in the animal preparation suggest that the QRS changes are due to conduction delay in the ischemic myocardium (1).

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We now extend these studies to patients during the first 5 h of acute myocardial infarction. In these patients we correlate the QRS changes with anatomic information obtained by coronary arteriography. The purpose of this study is to characterize the electrocardiographic (ECG) changes early in infarction that chiefly affect the terminal portion of the QRS complex and to demonstrate that analysis of these changes can provide information regarding the location of the ischemic region.

Methods

Patient selection. Patients with acute myocardial infarction were included in this study if they had an ECG taken within 5 h of the onset of chest pain and had an ECG taken before the acute infarction that was available for comparison. Data from 32 patients were analyzed. Twenty-two

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patients had an acute inferior myocardial infarction, nine had an acute anterior infarction and one patient had an inferior infarction followed in 5 days by an acute anterior infarction. Diagnostic criteria for infarction included elevation of total serum creatine kinase (CK) with an increased MB CK fraction, ST segment elevation of ≥0.1 mV and the appearance of abnormal Q waves within 24 h after admission. There were 27 men and 5 women in the study and their average age was 60 ± 9 years. Coronary anteriography was performed within 3 weeks of the acute infarction in 30 of the patients. No patient received thrombolytic agents or coronary angioplasty before the initial ECG during infarction.

Electrocardiographic analysis. The R wave and S wave amplitude in each lead and the largest ST segment deflection were measured in the baseline and early infarction ECGs from each patient. The difference in amplitude of the corresponding components was then determined. If more than one R wave peak was present, the largest amplitude was taken as the measurement for that lead. Only ECGs with adequate calibration pulses were analyzed. In the baseline tracing of seven patients, minor downsloping ST depression was noted and in five patients T wave inversion in leads III and aVF was present. There was no history of prior myocardial infarction in these patients. Two of the 32 patients had a history of a prior infarction; the baseline tracing in one of these patients demonstrated mild lateral ST depression and small inferior Q waves. The only finding in the baseline tracing of the other patient was an abnormal R wave/S wave ratio in lead V_1.

Statistical methods. An analysis of variance was performed on the 25 measurements from the preinfarction baseline ECG and the ECG obtained during acute myocardial infarction. After it was determined from the analysis of variance that significant changes in the measurements occurred between baseline and acute infarction, post hoc comparisons for the individual leads were done with Bonferroni's multiple comparisons test (2). This stringent statistical model was chosen to lessen the possibility of chance indications of statistical significance that might occur with this large number of post hoc comparisons. In the patients with anterior infarction, analysis of variance was performed to assess the significance of the interaction between the direction of change of R wave amplitude and the occurrence of the R wave early or late in the QRS complex. Throughout this report measurements are presented as mean values ± standard deviation.

Results

Patients with acute inferior myocardial infarction. In the 23 patients in this group the initial ECG was performed an average of 121 ± 98 min after the onset of chest pain. A representative set of ECGs from a patient in this group is shown in Figure 1; the baseline tracing (1A) was taken before the acute infarction and 1B was taken 20 min after the onset of chest pain. Subsequent ECGs showed changes that were typical of an inferior myocardial infarction, and coronary arteriography revealed an occluded right coronary artery and a normal left coronary artery system. In Figure 1B, the tracing taken during the infarction, reversal of the polarity of the terminal component of the QRS has occurred in leads II, III and aVF. The negative terminal deflection (S wave) present in the baseline ECG has changed to a large positive deflection. The small S wave in lead aVL has become deeper in the ECG during infarction. In addition, there is ST depression in the precordial leads and the amplitude of the S wave in leads V_1 to V_3 has increased (become more negative).

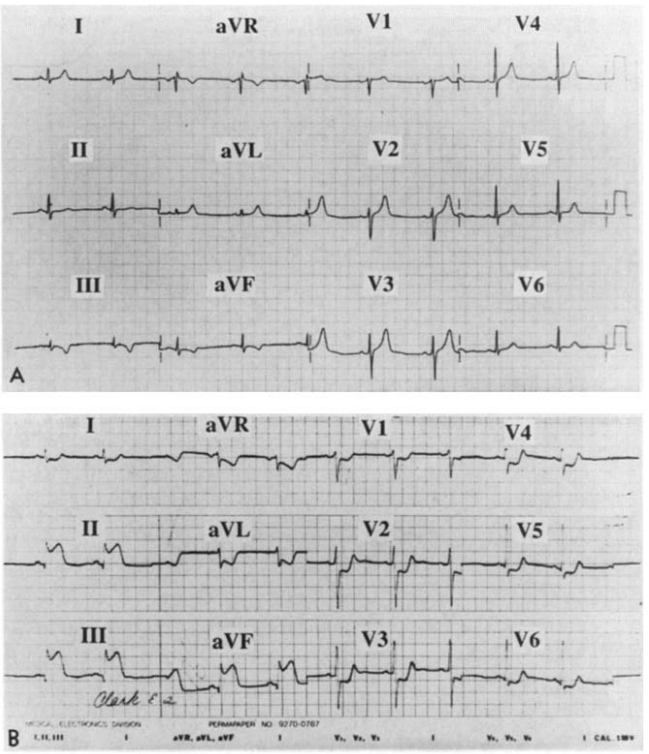


Figure 1. A, The preinfarction electrocardiogram (ECG). B, ECG taken 20 min after the onset of chest pain. In addition to signs of acute inferior infarction, the ECG shows that the negative terminal deflection (S wave) in leads II, III and aVF has changed to a large positive deflection. There is also ST depression in the precordial leads and the amplitude of the S wave in leads V_2 to V_3 has increased (become more negative). Angiographic findings in this case are described in the text.

Statistical analysis of the R wave and S wave amplitude in the 23 patients with inferior myocardial infarction demonstrated that the changes from baseline are of statistical significance ($p < 0.05$) in leads III, aVL and aVF (Fig. 2). Specifically, the R wave of lead III increased by 0.47 ± 0.35 mV, the S wave of lead aVL increased by 0.31 ± 0.23 mV

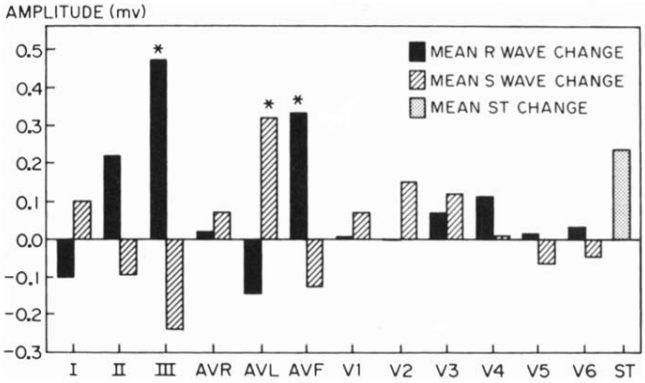


Figure 2. Changes in the mean amplitude of the R and S waves in 23 patients with acute inferior myocardial infarction. An **asterisk** is used to denote the electrocardiographic (ECG) components that showed a statistically significant change from the baseline ECG.

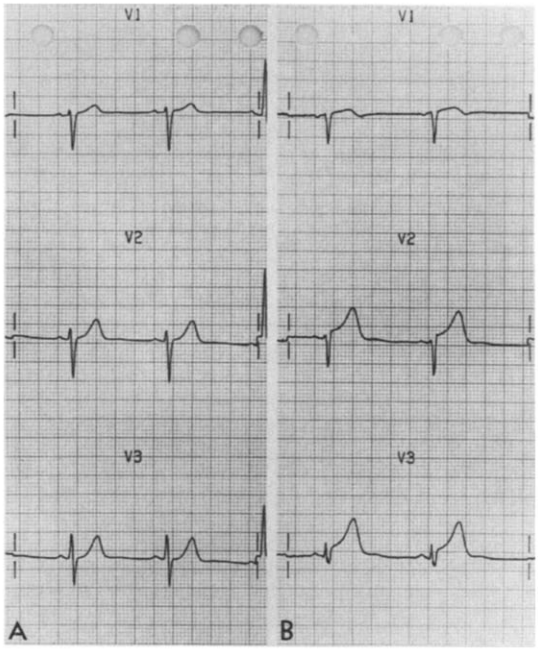


Figure 3. A patient who had an acute anterior infarction. **A**, The preinfarction electrocardiogram (ECG). **B**, The first ECG taken after the onset of chest pain. The infarction tracing shows ST elevation in leads V_1 to V_3 and decreased S wave amplitude (more positive) in these leads.

and the R wave of lead aVF increased by 0.37 ± 0.30 mV. Although the ST segment increased by an average of 0.23 ± 0.15 mV, this change was not statistically significant by the stringent test that was used for this assessment. The changes observed were also qualitatively uniform in that increases ≥0.1 mV occurred in these QRS components of leads III, aVL and aVF in 22 of the 23 patients with inferior myocardial infarction. Only 8 of the 23 patients were found to have new Q waves >0.1 mV in the initial tracing during infarction, a finding that may reflect the fact that the ECGs were obtained very early during the course of the acute infarction.

The time of occurrence of the R wave peak in leads III and aVF was estimated to the nearest 10 ms and the R wave maxima for the 23 patients with inferior infarction occurred at 50 ± 14 and at 53 ± 18 ms, respectively, in these leads. These measurements from leads III and aVF may not accurately determine the time of the QRS changes relative to the onset of ventricular activation because the contribution of the interventricular septum may not be evident in the inferior leads. Thus, the first deflection of the QRS in leads III and aVF may be relatively late in ventricular activation and our measurements should provide a minimal estimate of the time of occurrence of the changes. The fact that the S wave is the QRS component that is altered in lead aVL is another indication of the relative lateness of the change during ventricular activation. The R wave changes in lead III correlated highly with changes in the S wave in lead aVL (r = 0.94) as did changes in the R wave in lead aVF and the S wave in lead aVL (r = 0.91); these data added to the probability that we were measuring two expressions of the same phenomenon that affected the terminal portion of the QRS complex. In 18 of the 23 patients with inferior myocardial infarction, S waves were present in lead III or aVF of the preinfarction tracing and 17 of these patients lost the S wave completely in lead III or aVF or both. The single patient whose S wave persisted had a decrease in S wave amplitude of 0.4 mV in leads III and aVF. These changes in the late components of the QRS in leads III, aVF and aVL conceptually can be represented by a QRS vector that is directed inferiorly toward the ischemic zone during the early hours of acute myocardial infarction.

A third ECG taken within 48 h of the onset of chest pain (mean time 23.2 h) was available from 12 patients with inferior infarction. The R wave amplitude in lead III in the later postinfarction tracing was not significantly different from that in the preinfarction ECG (0.28 ± 0.20 versus 0.26 ± 0.15 mV; p = NS) in these patients.

Patients with acute anterior myocardial infarction. In the 10 patients in this group, the initial tracing was obtained 62 ± 58 min after the onset of chest pain. Figure 3 is a representative set of ECGs from a patient in this group; precordial leads V_1, V_2 and V_3 from the preinfarction baseline tracing (3A) are compared with the corresponding leads from the initial ECG during infarction (3B). In Figure 3B, the S waves in leads V_2 and V_3 have decreased in amplitude and the early R waves in leads V_2 and V_3 have also decreased. The tracings from another patient from this group are illustrated in Figure 4. In the baseline tracing (4A) the terminal component in leads V_1, V_2 and V_3 is negative. In the acute tracing (4B), marked ST segment elevation is present and the terminal component of the QRS in leads V_2 and V_3 is now a

JACC Vol. 14, No. 1
July 1989:143–9

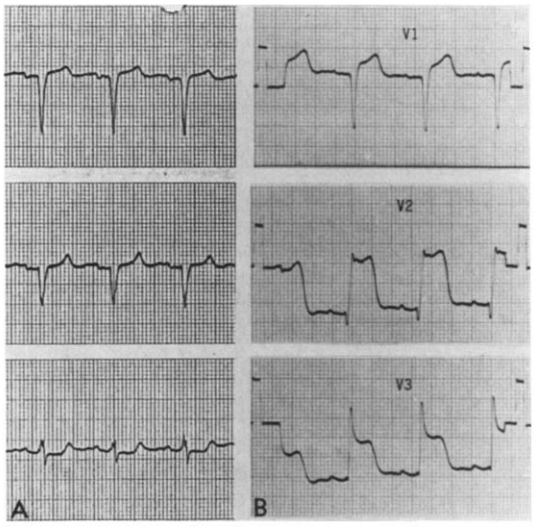


Figure 4. In this set of electrocardiograms (leads V_1 to V_3) from a patient with acute anterior infarction, there is striking ST elevation in leads V_1 to V_3 (**B**). In addition, the terminal portion of the QRS complex in leads V_2 and V_3 has changed from a negative deflection (**A**) to a positive deflection of much greater amplitude (**B**).

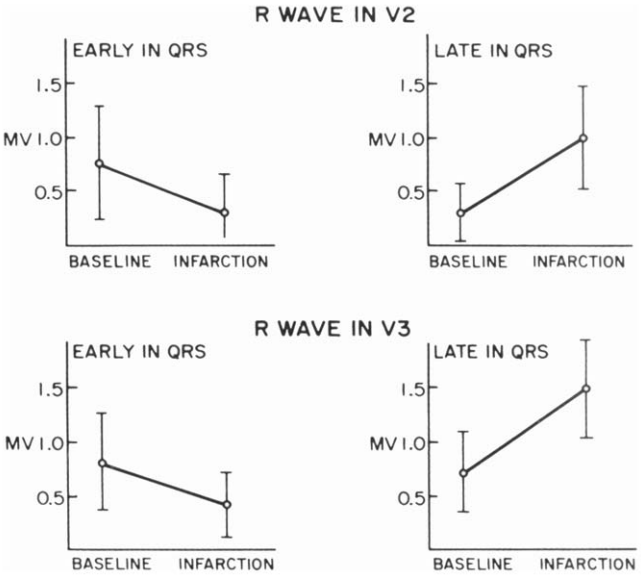
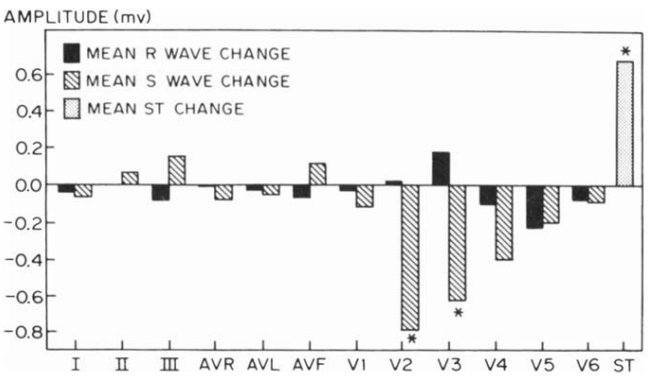


Figure 6. In the 10 patients with acute anterior infarction, the amplitude of the initial R wave decreased in leads V_2 and V_3 and the amplitude of the terminal R wave increased in these leads.

large positive deflection; the S wave amplitude has also decreased in the same leads. An analysis of the mean R wave and S wave changes in this group (Fig. 5) showed that there are statistically significant decreases in the S wave in leads V_2 (0.80 ± 0.50 mV, $p < 0.05$) and V_3 (0.64 ± 0.43 mV, $p < 0.05$). The ST segment was also found to increase by 0.67 ± 0.66 mV ($p < 0.05$). Similar directional changes of these variables were present in all patients in this group.

The direction and timing of the R wave changes in leads V_2 and V_3 were analyzed by noting whether the change occurred within the first 40 ms of the QRS complex or later. Analysis of variance revealed a significant interaction between the direction of change of the R wave amplitude and the relative time of occurrence of the change ($F[1,16] = 8.3$, $p < 0.01$). The amplitude of the early R wave decreased in leads V_2 and V_3 and the amplitude of the late R wave increased during infarction (Fig. 6). New Q waves with an area ≥1.0 mm^2 were noted in 2 of the 10 patients, and 5 of the 10 patients were found to have new Q waves of any size in the initial tracing during acute infarction. As with inferior myocardial infarction, the major changes occurred relatively late in the QRS complex and the direction of the QRS change could be represented by a late QRS vector directed toward the ischemic zone.

Figure 5. Changes in the mean amplitude of the R and S waves in 10 patients with acute anterior myocardial infarction. An **asterisk** is used to denote the electrocardiographic (ECG) components that showed a statistically significant change from the baseline ECG.



A third ECG taken within 48 h of the onset of chest pain (mean time 12.8 h) was available from seven patients with anterior infarction. The S wave amplitude in lead V_2 in the postinfarction tracing was not significantly different from that in the preinfarction ECG (1.2 ± 0.45 versus 1.5 ± 0.55 mV, p = NS).

Acute inferior infarction with ST depression in the anterior precordial leads. Seventeen of the 23 patients with acute inferior myocardial infarction had ST segment depression ≥0.1 mV in lead V_2 or V_3. Coronary arteriographic data were available for 22 of these patients and the patient who did not have coronary arteriography had a radionuclide ventriculogram during the acute infarction. Eight patients were found to have normal left main and left anterior descending coronary arteries. These patients were considered to have a low probability of having coexisting anterior ischemia during the acute inferior infarction and are classified as subgroup A. Seven patients had a ≥70% narrowing of the luminal diameter of the left anterior descending artery or

Table 1. Directional Change in S Wave Amplitude in 16 Patients With Acute Inferior Infarction and ST Depression in Anterior Precordial Leads

	S Wave in Lead V_2		S Wave in Lead V_3	
	Increase	Decrease	Increase	Decrease
Subgroup A	8	0	8	0
Subgroup B	4	4	4	4

Subgroup A = patients with normal left main and left anterior descending coronary arteries; Subgroup B = patients with 70% narrowing of the luminal diameter of the left anterior descending artery or a major diagonal branch.

a major diagonal branch and are classified as subgroup B. The patient who had a radionuclide ventriculogram (but not coronary arteriography) was found to have severe hypokinesia of the septal, apical and inferolateral regions with an ejection fraction of 27%; there was no history of a prior anterior myocardial infarction. Accordingly, this patient was included in subgroup B. The eight patients in subgroup B were considered to have an increased potential for anterior ischemia coexistent with the acute inferior myocardial infarction. One patient with ST segment depression in the anterior precordial leads during the acute inferior infarction had a 30% stenosis of the left anterior descending artery and was not included in this subgroup analysis.

The average ST depression in subgroup A was 0.26 ± 0.07 mV in lead V_2 and 0.22 ± 0.12 mV in lead V_3. In subgroup B, the average ST depression was 0.22 ± 0.21 in lead V_2 and 0.11 ± 0.05 mV in lead V_3. In subgroup A the magnitude of the S wave increased in lead V_2 by 0.33 ± 0.27 mV and in lead V_3 by 0.37 ± 0.24 mV. In Figure 1, from a patient in subgroup A, the S waves in leads V_2 and V_3 are deeper in Fig. 1B, the tracing taken during acute infarction. In subgroup B, the S wave amplitude decreased by 0.09 ± 0.56 mV in lead V_2 and 0.02 ± 0.67 mV in lead V_3. In Table 1 the directional changes in the S wave in leads V_2 and V_3 are summarized for both subgroups. It can be seen that the S wave consistently increased in leads V_2 and V_3 in subgroup A, whereas the direction of the S wave change was variable in members of subgroup B. Thus, the small mean change in the S wave in leads V_2 and V_3 of subgroup B is actually the net effect of two divergent trends; half of the members of subgroup B had an increase and the other half had a decrease in the S wave amplitude in leads V_2 and V_3. We infer from these observations that posterior ischemia may cause deeper S waves in the anterior precordial leads in subgroup A and that the ST segment depression was due to the ischemic process affecting the posterior regions of the left ventricle. This is supported by the arteriographic findings in this group. In subgroup B, which had an increased potential for coexisting anterior ischemia, there was a variable response of the S wave amplitude. We postulate that in the patients whose S waves became smaller (terminal QRS vector directed more anteriorly) there was coexisting anterior ischemia, whereas in the patients with increasing S waves (vector directed posteriorly) the changes are due to posterior ischemic injury associated with the inferior myocardial infarction. Two of the four patients in subgroup B who exhibited decreasing S wave amplitude in leads V_2 and V_3 subsequently had anterior infarction and died during the initial hospitalization. Only one early death occurred in the other 19 patients with acute inferior infarction.

Discussion

The time-honored approach to the interpretation of the ECG during acute myocardial infarction is to examine the tracing for the presence of ST segment displacement and to analyze the initial 40 ms of the QRS complex for the appearance of Q waves. Our observations indicate that predictable changes occur in the terminal portion of the QRS complex during the early phase of acute myocardial infarction. Common to each patient in our study groups is a change that conceptually can be represented by a vector late in the QRS complex that is directed toward the ischemic zone. In inferior infarction the terminal component of the QRS complex shows the most marked changes in leads III, aVF and aVL, and in anterior infarction the terminal component of the QRS in lead V_2 and lead V_3 usually shows the most marked changes.

Causative mechanisms. Detailed ECG studies (1) during myocardial ischemia in patients with variant angina pectoris have shown similar QRS changes late in the QRS complex. In animal models of transient ischemia the QRS changes were temporally related to delayed epicardial activation and a decrease in conduction velocity in the ischemic zone (1,3,4). It is recognized that the amplitude and configuration of the QRS complex are influenced by strong mutual cancellation and any condition that alters the sequence of ventricular depolarization to reduce this cancellation would produce an increase in the magnitude of the potentials recorded in one or more leads (3,5). With the development of ischemia, the delayed depolarization in the ischemic zone would be relatively unopposed and could account for the increase in the voltage of the terminal portion of the QRS.

A second related mechanism that may be operative during ischemia is that the pathway of depolarization from the endocardium to the epicardium may change from a direction that is tangential to the endocardium to a more radial direction and increase the amplitude of the QRS complex (3). Also, according to Durrer and van der Twell (6), the widespread Purkinje fiber ramifications in the inner layers of the heart cause wave front cancellation; slight changes in the activation process of the subepicardial layers such as those produced by ischemia would be expected to have considerable influence on the height of the R wave.

Comparison with previous studies. Changes in R wave amplitude during infarction have been noted by others (7–10) and a variety of ventricular conduction defects have been described (11,12). First et al. (11) described a group of patients with QRS prolongation (duration >0.12 s) and introduced the term periinfarction block. Grant (12) defined the basic features of periinfarction block as 1) an abnormality of the direction of initial forces of the QRS complex of a type characteristic of myocardial infarction; 2) an abnormality of the direction of the late forces of the QRS complex so that they point opposite to the initial QRS forces; and 3) little or no prolongation of the QRS complex. He concluded that periinfarction block is seen nearly exclusively with anterolateral and diaphragmatic infarction and he postulated that the ECG change was due to block in divisions of the left bundle branch. The changes described by Grant persisted after the acute phase of the infarction and he estimated that no more than 2% of patients eventually lost the terminal QRS abnormality (12). Virtually every patient in his series of patients with terminal QRS abnormalities also had Q waves. Although there are some morphologic similarities between the changes that we now describe and those reported by Grant, there are major differences in the two ECG phenomena. First, the ECG changes that we have observed occur during the first 5 h of the myocardial infarction and typically occur before the appearance of a Q wave. Second, the terminal changes in the QRS complex seldom persist.

In animal studies (1) in which myocardial ischemia is associated with epicardial and surface QRS changes there is a 30 to 40 ms delay in epicardial activation in the ischemic zone, but endocardial activation is virtually unchanged. In an experimental model of chronic infarction, Daniel et al. (13) showed that epicardial delay was due to slowed intramyocardial activation rather than to delay in Purkinje fiber conduction. Correlations between electrical and anatomic data in two patients suggested that, within limits, the detailed relations between the infarct and the activation sequence established with the canine model could be applied to human infarction (13).

Clinical implications. Our observations imply that analysis of the changes in the terminal portion of the QRS complex can aid in determining the location of the ischemic zone early in the course of a myocardial infarction. Although in many infarcts the location of the ischemic zone can be determined by analysis of the ST segment displacement, the additional information gained from analysis of the terminal part of the QRS complex may have particular clinical relevance when an acute inferior infarction is accompanied by ST segment depression in the anterior precordial leads. In this case the ST segment depression may be a reciprocal ECG effect attributable to ischemic injury of the posterior myocardium or, alternatively, to coexisting ischemia of the anterior wall of the left ventricle. Analysis of our subgroup of patients with inferior myocardial infarction, ST depression in anterior precordial leads, and no obstructive lesions in the anterior descending coronary artery showed consistent deepening of the S waves in leads V_2 and V_3. The subgroup of patients with inferior infarction, ST depression in anterior leads and a severe obstructive lesion in the anterior descending artery showed variable responses in the S wave of leads V_2 and V_3. Lacking an independent measure of myocardial ischemia, we can infer, but not rigorously prove, that decreased S wave amplitude was an indication of anterior ischemia in these patients.

Limitations of the method. The practical limitation of the use of terminal QRS complex analysis to determine the location of the ischemic zone in acute infarction is the lack of a preinfarction ECG that is technically comparable with the tracing taken during myocardial infarction. Technical factors such as inconsistent precordial electrode placement may produce QRS changes that are greater than those caused by the infarction.

Conclusions. Predictable changes in the terminal portion of the QRS complex occur early in the course of acute myocardial infarction. These changes are similar to the QRS changes that have been observed in animal experiments and are attributed to decreased conduction velocity in the ischemic region. When a preinfarction ECG is available that is technically comparable with the ECG taken during infarction, analysis of the QRS changes may provide information regarding the location of the ischemic zone.

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